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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/652,493 08/31/00 BISSELL

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EXAMINER

DAVIS, N

ART UNIT

PAPER NUMBER

1642

DATE MAILED:

10/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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Office Action Summary

Application No.

09/652,493

Applicant(s)

BISSELL ET AL.

Examiner

Natalie A. Davis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 14 November 2000.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 and 22-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 22-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

The Group Art Unit examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to **Dr. Natalie A. Davis**.

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 1-4, drawn to a method of detecting the presence of a fragment of α -dystroglycan, classified in class 435, subclass 7.2.
 - II. Claims 5-8, drawn to a method of detecting the full-length α -dystroglycan, classified in class 435, subclass 7.2
 - III. Claims 9-12, drawn to an assay for identifying inhibitors of metalloproteinase which specifically cleaves α -dystroglycan from the cell surface, classified in class 435, subclass 7.2.
 - IV. Claims 13-21, drawn to a method of suppressing mammalian tumor cell growth, classified in class 424, subclass 184.
 - V. Claims 22-24, drawn to a method of assaying proteolysed α -dystroglycan fragments, classified in class 435, subclass 7.8.
 - VI. Claim 25, drawn to a method of restoring normal dystroglycan function, classified in class 424, subclass 93.2.
 - VII. Claims 26-28, drawn to an assay for identifying metalloproteinase inhibitors, classified in class 435, subclass 7.1.
2. The methods of Groups III-IV and VI-VII relate to methods but each method differs in method steps, modes of operation, reagents needed and serve different endpoints and effects.
3. Because these inventions are distinct for the reasons given above and require different search strategies, restriction for examination purposes as indicated is proper.

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4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

6. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

7. The previous examiner (Matthew Owens) during a telephone conversation with Attorney Mahoney a provisional election was made without traverse to prosecute the invention of Groups I, II, and V, claims 1-8 and 22-24. Affirmation of this election must be made by applicant in replying to this Office action. Claims 9-21 and 25-28 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Information Disclosure Statement

8. The information disclosure statement filed 31 August 2000 has been considered. A signed copy is attached hereto.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are drawn to a method for measuring potential tumorigenicity of cells comprising detecting the presence of α -dystroglycan in medium containing a tissue or cells, whereby the presence of the fragment indicates higher potential tumorigenicity. The claims are further drawn to detecting the presence of the α -dystroglycan fragment using a monoclonal antibody of laminin and measuring the size of the fragment and detecting the amount of α -dystroglycan relative to β -dystroglycan, wherein a decrease in α -dystroglycan indicates higher potential tumorigenicity.

The specification defines a cell, which possesses tumorigenicity as a cell lacking normal growth arresting characteristics, normal non-tumorigenic cells as polarized (mammary cells form acini and have regulated growth properties), and tumor cells as disorganized, which exhibit abnormal growth and are sometimes invasive (page 4). The disclosure indicates that many tumor cells do not have normal α -dystroglycan on the surface and thus lack dystroglycan function and conclude that dystroglycan is a tumor suppressor (page 5). In addition, cells lacking a tumor suppressor function are disclosed as having higher "potential tumorigenicity" (page 5). The specification further states that inhibition of dystroglycan binding to laminin permits cell spreading and growth in the presence of laminin as normally cells in the presence of laminin round-up and growth arrest (page 9). Finally, the specification exemplifies that tumorigenic

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cells overexpressing dystroglycan round up in response to laminin and are no longer capable of producing tumors when injected into mice (pages 24-25).

11. The instant disclosure fails to meet the enablement requirement for the following reasons:

Matsumura et al. (J Biol. Chem., 1997, 272(21) 13904-13910) is cited in order to establish the general state of the art and level of predictability of dystroglycan. Matsumura et al. teach the role of dystroglycan in cell adhesion. Matsumura et al. teach a dystroglycan complex, which comprises α - and β -dystroglycan and laminin in the surface membrane of rat schwannoma cell line RT4 and the presence of α -dystroglycan in culture medium, suggesting that α -dystroglycan is secreted. Furthermore, RT4 cells cultured in the presence of dystroglycan on dishes coated with laminin-1 became spindle shaped and adhered to the bottom surface, whereas cells cultured under the same conditions in the presence of monoclonal antibody to α -dystroglycan remained round and did not adhere to the surface. Durbeej, et al. and Henry, et al. teach a role of dystroglycan in the assembly of basement membranes in developing tissue. There is no record in the art teaching dystroglycan as a tumor suppressor.

The specification does not disclose whether a mutated form of the dystroglycan gene results in cancer, it only discloses many tumor cells do not have normal α -dystroglycan on the surface and thus lack dystroglycan function. Additionally, it does not define dystroglycan function beyond that of its ability to bind laminin and there is no art on record that discloses its role in tumor suppression or any correlation of its expression levels to tumorigenicity. Since there is no evidence in the art teaching α -dystroglycan expression levels and its correlation with tumorigenicity, it would be unpredictable to measure potential tumorigenicity based on α -dystroglycan measurements. In addition, the specification does not provide guidance as to what level of α -dystroglycan would constitute abnormal levels and how these levels would be indicative of potential tumorigenicity. The disclosure only shows tumorigenic cells overexpressing dystroglycan round up in response to laminin and are no longer capable of producing tumors when injected into mice, but does not give any definitive evidence that measurement of α -dystroglycan is indicative of potential tumorigenicity. Until some substantial evidence, as indicated above, can be attributed to the claimed method, one of ordinary skill in the

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art would be required to perform undue experimentation in order to practice the invention as claimed.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coico, et al., (1991, Current Protocols in Immunology) and further in view of Matsumura, et al. (1993).

The claims are drawn to a method of assaying proteolysed α -dystroglycan fragments in blood serum comprising contacting a sample with a labeled antibody specific for an α -dystroglycan fragment and assaying the amount of bound label, wherein the fragment is approximately 120 or 60 KD.

Coico, et al. teach an ELISA method of detecting for the presence of an antigen comprising contacting a sample with a labeled antibody specific for that antigen. Coico, et al. does not teach α -dystroglycan fragments that are approximately 120 and 60 KD and antibodies that specifically bind to those fragments. However, Matsumura, et al. teach α -dystroglycan fragments that are approximately 120 and 60 KD and antibodies that specifically bind to those fragments. Since Coico, et al. teach the assay method as claimed and Matsumura, et al. teach the fragments and antibodies to be used in the method, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings to use the method as claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Natalie A. Davis whose telephone number is 703-308-6410. The examiner can normally be reached on M-F 8-5:30 (every other Friday off).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4315 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Natalie A. Davis, Ph.D.
September 27, 2001


ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
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